Vision and health related quality of life in immunO suppressive treated uveitic population

Dissertation submitted for

M.S. (Branch III) Ophthalmology

The Tamilnadu Dr. M.G.R. Medical University, Chennai

ΦΕΒΡΥΑΡΨ 2006

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by

DR. N. SATHIAN

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Χερτιφιχατε

Certified that this dissertation entitled "VISION AND HEALTH RELATED QUALITY OF LIFE IN IMMUNO SUPPRESSIVE TREATED UVEITIC POPULATION" ***submitted for M.S. (Branch III) Ophthalmology, February 2006 to The Tamilnadu Dr. M.G.R. Medical University, is the bonafide work done by*** Dr.N. SATHIAN ***under our supervision and guidance in the Department of Uvea at Aravind Eye Hospital and Post Graduate Institute of Ophthalmology, Madurai, during his residency period from April 2003 to March 2006.***

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Αχκνοωλεδγεμεντ

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Contents

PART – I

INTRODUCTION

Until the last couple of decades, assessment of medical outcomes was strongly focused on gains in survival time, (i.e.) Quality of life. To most people, “Quality of life” refers to how good, desirable and enjoyable life as a whole is felt by the person in question[1].

The impact of chronic eye disease causing severe visual impairment has been evaluated by objective means and has been considered infallible. Patients with these chronic eye diseases are treated with various methods and resolution of pathological process is expected out of it, from physician's point of view. But, the real purpose of managing a chronic eye disease is to restore lost vision and to satisfy the patient as a whole with minimal adverse effects.

In ophthalmology, the above quality of life and visual functions has been assessed with visual function assessment questionnaires (IND-VFQ / NEI VFQ) for many disease like cataract, ARMD[2], glaucoma[3], low vision patients[4], surgical procedures likes ECCE Vs ICCE[5,6,7,8] but the impact on health related quality of life following treatment in patients with chronic eye disease merits more detailed evaluation.

Over the past decade, ophthalmic clinical trails are increasingly incorporating patient – perceived general health related and vision specific quality of life (QOL) instruments as secondary outcome measures. The advantage of including a general health related QOL instrument along with disease specific instruments is that a general QOL instrument provides an important content for interpreting the disease specific data[9].

Hence, it was decided to analyze vision and health related quality of life in immunosuppressive treated uveitic patients and to verify the effect of treatment in the same population.

QUALITY OF LIFE

The quality of life is strictly a personalized issue. Thus there is a strong argument that health related quality of life measurement should be based on patients defined issues[10].

The health is just not absence of disease. It also involves social and psychological well being. So, when we analyze that, the concept of well being of an individual or group of individuals have objective and subjective components.

- **Objective components**
    1. Standard of living (refers to the usual scale of our expenditure, the goods we consume and the services we enjoy)
    2. Level of living (it consists of nine components like health, food consumption, education, occupation etc)
- **Subjective components**

    Quality of life

So, quality of life is a subjective well-being and it was defined by **WHO**[11] as:

"The condition of life resulting from the combination of effects of the complete range of factors such as those determining health

happiness (including comfort in the physical environment and satisfying occupation) education, social and intellectual attainments, freedom of action, justice and freedom of expression.

It is “an individual’s perception of their position in life in the content of culture and value systems in which they live and in relation to their goals, expectations, standards and concerns[12].

Now a days people demand higher quality of life, which determines a persons satisfaction and it will be the ultimate goal of any treatment initiative.

Hence there is a need for quality of life studies to find out, if our treatment increases the quality of life[13] in all situations and if not think about remedial measures or alternative modalities.

QUALITY OF LIFE INSTRUMENTS

QOL instruments are important tools that can complement and enhance the value of traditionally accepted test of outcome in the evaluation of clinical interventions[14].

QOL measures have become the standard means of assessing the results of health care interventions and more controversially, the means of prioritizing fundings[15].

QOL instruments fall into two categories[16].

* **Generic** : which are broadly applicable across disease state and severities

* **Disease specific** : which are designed to evaluate specific diagnostic states or patient populations.

Though it is easy to say that QOL assessment can be done by questions, it had many hurdles and many of them had been addressed to make the questionnaire a reliable modality.

The difficulties encountered are[17,18,19] :

a. what questions to be asked
b. How many questions
c. in what type of format
d. Can it be used in a wide range of situations.

Steps in Development of QOL instrument

Step I : Generation of relevant issues

Step II :

Issues are converted into questions to get a dichotomous or polytomous response.

Each item is assigned a numerical score that corresponds to the rank of the patients response.

Step III

Grouping of items into different domains is thus based on developers own judgement[20,21] on the basis of principal component analysis or reinforced with confirmatory factor analysis.

Principal component analysis and factor analysis are used to look at the correlations of responses among items in the instrument.

If correlation is high, they probably assess the same variables. If low then they are most likely to assess different variables.

Thus different items are grouped to form domains.

Step IV

Developing a scoring scale for each domain. Summary scores are developed for each domain by summing or averaging item scores.

The domain scores and instrument scores are called raw scores, which are treated as literal measurement scales.

Raw scores are converted into norms to allow comparison between individual performances with the performance distribution in the population. Then scales are tested for validity.

Over all instrument scores is a sum or average of domain scores.

DEFINITION OF TERMS

Instrument

The set of questions used to assess daily functionary or other aspects of health related quality of life is called an instrument.

Items

Individual questions in the instrument.

Dichotomous Rating

Patient is made to answer either true or false.

Polytomous Rating[22]

Patient is made to answer from a list. eg. choosing a response out of a list of ordered categories such as ratings of difficulty or frequency on a scale from 1 to 5.

Domains or Subscales

The items in a questionnaire instrument might be grouped into domains or subscales each consisting of items, which are related and are assessing the same variable (eg. : distance vision, driving etc).

NATIONAL EYE INSTITUTE – VISUAL FUNCTION QUESTIONNAIRE

National eye institute questionnaire, a targeted multi-dimensional survey, was designed to represent the perspective of the patient with respect to visual disabilities and their impact on daily functioning.

The initial version of NEI – VFQ had 51 questions which represented 13 different subscales. Despite the success of the longer field test version and its continued use, to enhance feasibility, a short version was planned.

Development of NEI –VFQ – 25[23]

National eye institute sponsored the development of the VFQ-25 with the goal of creating a survey that would measure the dimensions of self-reported vision targeted health status that are most important for persons who have chronic eye diseases.

Because of this goal, the survey measures the influence of visual disability and visual symptoms on generic health domains such as emotional well being and social functioning, in addition to task – oriented domains related to daily visual functioning.

NEI – VFQ – 25 is the product of an item reduction analysis of NEI – VFQ – 51. It differs from the previous version by two things.

1. It includes an extra driving item from the appendix of supplementary questions as part of the base set of items.
2. Also, the revised scoring algorithm excludes the single item general health rating question from the calculation of the vision targeted composite score.

Version 2000, the final version of the VFQ – 25 has the above difference from previous long versions (NEI – VFQ – 51)

Version 2000, has additional of 14 questions which can be added to make NEI – VFQ – 25 into a 39 item visual function questionnaire.

Item Reduction Guidelines[20]

The following qualitative criteria were used to identify candidate items for NEI–VFQ 25 survey. They are

1. Retained items should have low missing data rates. The inclusion of items that are most likely to be answered by most person will maximize the available information from each participants.
2. To maintain breath of content, the intent is to have all 51-item VFQ's constructs represented in the shorter survey, thereby remaining faithful to the range of topic areas mentioned by participants in the original focus groups.
3. Priority is placed on retaining items with approximately normal distributions of responses over those with skewed distribution (large ceiling or floor effects).

Once these 3 qualitative criteria are taken into consideration, the items that explain the greatest portion of variance for each of the original 51-item NEI – VFQ subscales in linear regression models are retained in the NEI – VFQ 25.

Reliability[24]

It is evaluated by estimating the internal consistency of the NEI – VFQ 25 which was calculated using Cronbach co-efficient α for each of the multi-item scales.

Internal consistency estimates for the NEI – VFQ 25 subscales ranged from 0.71 to 0.85 among persons with eye diseases while 51 item scale had internal consistency estimates greater than or equal to 0.70, indicating that the measure has acceptable reliability for group level comparisons.

Validity

Validity assesses how well a measure adequately represents the domains or construct of interest[20].

Correlations between the NEI – VFQ 25 versions of each subscale and their respective long term version were greater than 0.90[24].

On average, each NEI- VFQ – 25 subscale predicts 92% of the variance in the corresponding 51 item subscale score.[23]

Subscales

The VFQ – 25 consists of a base set of 25 vision target questions representing 11 vision related subscales, plus an additional single item general health rating question as shown in table 1(annexure)

All items in the VFQ – 25 are from the 51 item field test version; no new items were developed for use in the VFQ – 25.

The guiding principles for the selection of the short form items included:

1. Low item-level missing data rates
2. Normal distribution of response choices
3. Retention of items that explained the greatest proportion of variance in the 51 item subscales.

Format

National Eye Institute visual function questionnaire, 2000 version has two format.

1. Interviewer administered format
2. Self administered format

NEI – VFQ – 25 takes approximately 10 minutes on average to administer in the interviewer format.

The self administered version of the survey can also be used, however, its psychometric testing has not been done.

To ensure the comparability of scores across studies, it is our position that the order of items should not be changed.

The questionnaires were completed before the ophthalmic examination by the interviewer, to reduce the influence of the clinical encounter on patient responses.

Scoring

Scoring of NEI – VFQ – 25 with or without optional items is a two step process.

Step I

Original numeric values from the survey are re-coded following the scoring rules outlined in table 2(annexure).

All items are scored so that a high score represents better functioning. Each item is then converted to a 0 to 100 scale so that the lowest and highest possible scores are set at 0 and 100 points, respectively. In this format, scores represent the achieved percentage of the total possible score.

Step II

Items within each sub-scale are averaged[14] together to create the 12 subscale scores. Items that are left blank (missing data) are not taken into account when calculating the scale scores.

Subscales with at least one item answered can be used to generate a sub scale score. Hence, scores represent the average for all items in the sub scale that the respondent answered.

Response 6 indicates that the respondent does not perform the activity because of reasons that are unrelated to vision. If a respondent

selects this choice, the answer is treated as missing and an average of the remaining items is calculated.

Composite Score Calculation

To calculate an over-all composite score for the VFQ – 25, simply average the vision– targeted sub-scale scores, excluding the general health rating question.

By averaging the sub scale scores rather than the individual items, we have given equal weight to each sub scale, where as averaging the items would give more weight to scales with more items.

Formula[23]

$$\text{Mean} = \frac{\text{Score for each items with a non missing answer}}{\text{Total number of items with non missing answers}}$$

100 : Best possible score, 0 : Worst possible score

HEALTH RELATED QUALITY OF LIFE INSTRUMENT (SF 36/SF 12)

Over the past decade, ophthalmic clinical trials are increasingly incorporating patient – perceived general health related and vision specific quality of life (QOL) instruments as secondary outcome measures.

Health related QOL is a multidimensional concept that encompasses physical, emotional and social aspects associated within a

given disease or its treatment. Measurement of health related QOL can provide helpful supplementary information on patient outcomes in the recovery process.

The advantage of including a general health – related QOL instrument along with disease specific instrument is that, a general QOL instrument provides an important context for interpreting the disease specific data.

The short form 36 (SF – 36) questionnaire is one of the most widely used health status evaluation tools. It is a generic instrument developed by J.WARE for assessing patients with chronic disease[25].

The SF – 36 consists of 36 questions, which require the respondent to rate items related to eight conceptual areas, including general health, ability to perform certain physical tasks, level of pain, emotional state and limitations in usual activities. The SF-36 can then generate two composite scores

- Physical composite scores (PCS)
- Mental composite score (MCS)

which provide an overall assessment of the respondent's physical and mental health.

Although very useful for a variety of health outcome evaluation purposes, the SF – 36 can take 10 to 12 minutes to complete. Because of its length, the SF 36 is frequently considered to be too long for

inclusion in clinical studies with large scale measurement and monitoring efforts.

An abbreviated version of the instrument containing a 12 question subset of the SF-36 was developed; its development was started in the New England Medical Center in the spring of 1994.

The SF–12 survey and scoring method was developed with the hope that, this shortened questionnaire could produce PCS and MCS composite scores that were comparable to the SF-36. The average time to complete the SF-12 questionnaire is reported to be less than 2 minutes.

Improved study efficiency and cost saving may be realized by using a shorter questionnaire to measure general health status.

The short form SF –12 health survey measures generic health concepts relevant across age, disease and treatment groups. It provides a comprehensive, psychometrically sound and efficient way to measure health from the patient's point of view by scoring standardized responses to standard questions.

The SF-12 includes 8 concepts commonly represented in health surveys: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role functioning, emotional and mental health. Results are expressed into terms of two Meta scores: the PCS - 12 and MCS-12.

Scoring of SF-12

The standardized response of each of the 12 questions in SF-12 has its own numerical score, details of which are included along with questionnaire in annexure.

To calculate PCS and MCS scores, scored test items are normalized in a computer algorithm that generally requires a computer.

The PCS and MCS scores have a range of 50 to 100 and were designed to have a mean score of 50 and a standard deviation of 10 in a representative sample. Thus, score greater than 50, represent above average health status.

On the other hand, people with a score of 40 function at a level lower than 84% of the population (one standard deviation) and people with a score less than 30 function at a level lower than approximately 98% of the population (two standard deviation).

As computer algorithm for normalizing the scores of PCS and MCS was not available, mean score of each subscale prior and after treatment were calculated and their significance tested by paired t-test value.

Compared with the SF-36, the disadvantages of using the SF-12 include less–precise estimate of individual health and an inability to calculate summary scores when first item is left unanswered[28].

Therefore, only patients who completed all of the SF-12 items were included in the statistical analysis.

Validity of SF –12

The relationship between the PCS – 12 and MCS – 12 scores with the PCS-36 and MCS –36 was assessed using the Pearson correlation co-efficient as a measure of criterion and discriminant validity.

Criterion Validity

Criterion validity refers to the correlation of a scale with an alternative measure of the trait or condition under study, ideally, a "gold standard' that has been used and accepted in the field[29].

No statistically significant difference were found between PCS and MCS scores from the SF – 36 compared with that of SF –12.

Discriminant Validity

Discriminant validity refers to the ability of a scale to demonstrate a higher correlation with its intended study sample than a separate and less specific scale with the same sample.

The PCS–12 and MCS–12 scores were highly correlated with similar indicators (composite scores and subscales) of the SF-36, which has been shown to be a reliable and valid standardized measure of QOL[30].

IMMUNOSUPPRESSIVES

Immunosuppressive agents by definition suppress development of at-least one type of immune reaction and they modify the specific immune sensitization of lymphoid cells. A common feature of this family of drugs is their ability to interfere with synthesis of nucleic acids and or proteins[31].

The major immunosuppressives used in uveitis was divided into alkylating agents and antimetabolites along with noncytotoxic immunosuppressive medications such as cyclosporine.

Immunosuppressive agent represents the final rung in our stepladder approach to the medical treatment of ocular inflammatory disease[32]. The safe use of these drugs begins with exclusion of infections, mechanical or other treatable causes of ocular inflammation.

Informed consent is obtained and documented; the patient is given an explanation of the potential risks and benefits involved in this therapeutic modality. Initially steroids are used in maximally tolerated doses.

The choice of the agent is individualized for each patient and depends on a variety of consideration, including the underlying disease, the patient's age and the medical status. Patients are carefully screened for risk factor which might preclude the use of certain immunosuppressives (e.g. Hepatic disease for methotrexate, and renal disease for cyclosporine).

Patients are also informed of the proper dosing and intake, potential adverse reactions and alternative to therapy.

Indication

Absolute : 1. Behcet's syndrome
2. Rheumatoid Sclero-uveitis

3. Sympathetic ophthalmia
4. VKH syndrome
5. Serpiginous choroidopathy

Relative : 1. Intermediate uveitis
2. Retinal vasculitis
3. Chronic cyclitis

Questionable : Children with intermediate uveitis

Guidelines

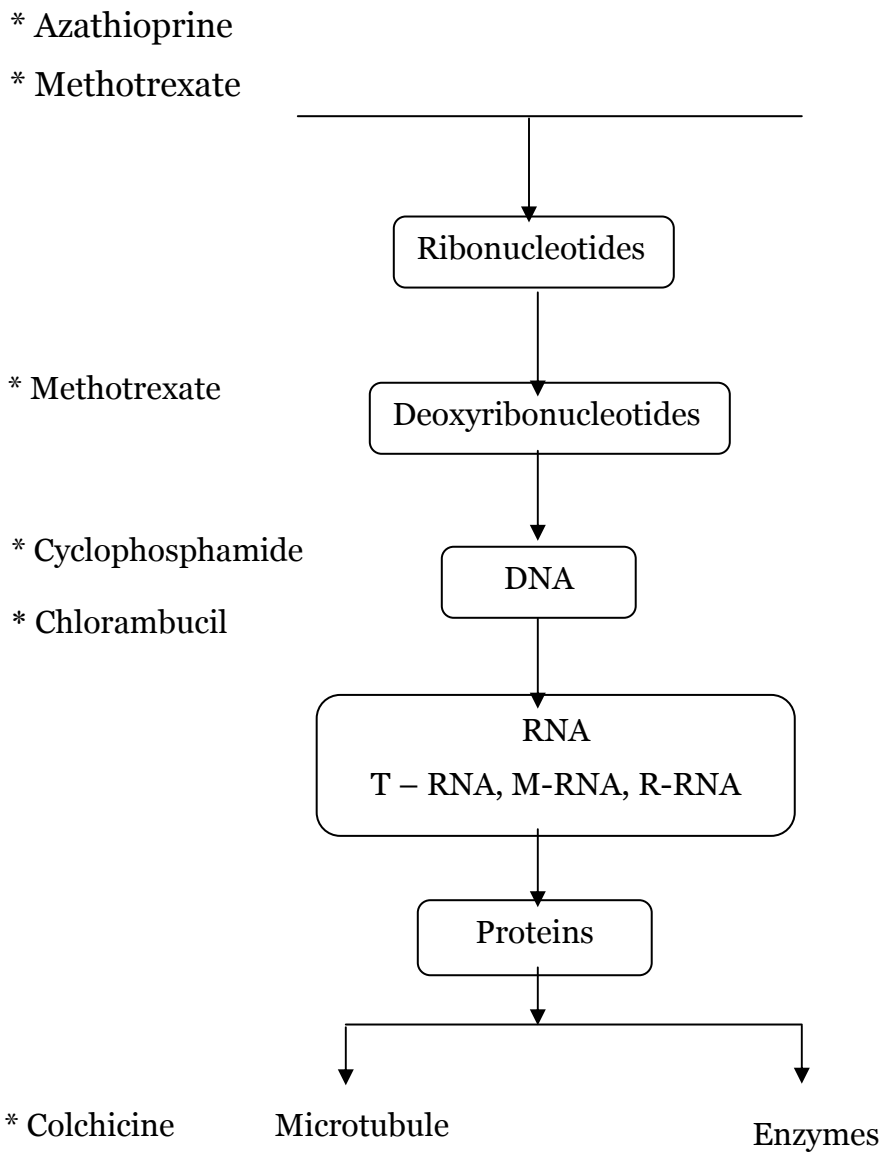
Prior to initiation of therapy with any cytotoxic agents, it is important to consider these guidelines.

1. Absence of infection / masquerade syndrome.
2. Absence of hematological contra-indications.
3. Meticulous follow up by ophthalmologist or internist or a medical oncologist, if necessary.
4. Objective evaluation of the disease process.
5. Informed consent.

Mode of Action

Immunosuppressive agents as by definition suppress development of at least one type of immune reaction. A common feature of this family of drugs is their ability to interfere with the synthesis of nucleic acids and / or proteins.

Purine synthesis Pyrimidine synthesis



STERIODS AS IMMUNOSUPPRESIVE

Corticosteroids are the mainstay of anti-inflammatory therapy for most types of uveitis, and effectively suppress the inflammatory response regardless of its cause.

Mechanism of Action

The anti-inflammatory effects are initiated when the corticosteroid molecule enter the target cell and combines with the

glucocorticoid receptor within the cytoplasm. This steroid receptor complex is then transported to the nucleus, affects the DNA transcription resulting in change in messenger RNA production, protein synthesis and cell function. Glucocorticoid receptors are present not only on all cells of the immune system but also in iris, ciliary body and corneoscleral tissue of eye.

Corticosteroids appear to act at the recognition and proliferative phase of immune response, therapy suppressing both B cell and T cell mediated response which eventually lead to impairment of both cell mediated immunity and humoral immunity.

Routes of Administration

Corticosteroids can be delivered to eye by three routes. Topical steroids which have a good therapeutic effect in anterior segment, have poor penetrance into posterior segment. In that instance, periocular steroid via posterior-subtenon deposteroid injection is being used to treat intermediate and posterior uveitis. Major disadvantage of this route is elevated intraocular pressure.

It is in case of bilateral uveitis or in patients who have severe unilateral inflammation and who are intolerant to or unresponsive to, periocular injections, systemic corticosteroids are employed.

Principles of systemic corticosteroid therapy in uveitis[32]

1. Use enough, soon enough, often enough and long enough to secure desired results.
2. Suppress inflammation until the pathogenic mechanism burn out. Increase dosage immediately if there is recrudescence.
3. If systemic therapy lasts for more than 2 weeks never stop abruptly at a higher dosage as it precipitates addisonian crisis – taper dose slowly.
4. Corticosteroid should not be used as the last resort; they should be started as soon as indicated.
5. One should start with a high dosage and taper.
6. The steroid dosage should not be tapered with a pre determined plan, but accordingly to the disease response.

Indications

Following are the ophthalmic indications for use of corticosteroids.

Eyelids

- Contact dermatitis
- Discoid lupus
- Chemical burns

Conjunctiva

- Allergic disease (vernal, GPC)
- Ocular cicatrical pemphigoid

Cornea

- Disciform keratitis
- In peripheral ulcerative keratitis
- Graft rejection
- chemical burns without epithelial defect

Sclera

- Scleritis

Orbit

- Pseudotumours
- Grave's orbitopathy

Uvea

- Anterior uveitis
- Pars planitis
- Posterior uveitis
- Sympathetic ophthalmia
- VKH syndrome
- Endophthalmitis

- Vasculitis / choroiditis

Retina

- Cystoid macular oedema
- Acute retinal necrosis

Neuro-opthal

- Optic neuritis
- Temporal arteritis
- Ocular myasthenia

Others

- Post operative
- Trauma

Contra Indications

➢ ***Absolute***

1. Known or suspected systemic fungal infections
2. Known hypersensitivity to steroid formulation
3. Systemic infections like toxoplasmosis, herpes and tuberculosis.

➢ ***Relative***

1. Severe cardiovascular disease
2. Psychiatric patients

3. Previous GI problem
4. Diabetic patients
5. Musculoskeletal disease
6. Pregnancy

Dosage

Dose of oral corticosteroids, which in excess of the daily endogenous output of hydrocortisone (about 20 mg), are necessary to produce the anti-inflammatory or immunosuppressive action. In this study, patients receiving steroid dose in excess of 1mg / kg/d is considered as immunosuppressive dosage and included in this study.

Initial dose	:	1mg/ kg/d
Max dose	:	60-80 mg/kg/d
Maintenance dose	:	≤10mg/d

Tapering

When high dose oral corticosteroids are given for more than 2 weeks, it should never be discontinued abruptly, as it precipitates an addisonian crisis.

A slow and steady tapering is done, at a rate dictated by the clinical condition, so that a recurrence of inflammation is not precipitated.

Tapering Schedule

Initial Dose	**Method of Tapering**

> 40 mg/d	:	decrease by 10mg / d ,every 1-2 weeks
40-20 mg/d	:	decrease by 5mg/d, every 1-2 weeks
20-10mg/d	:	decrease by 2.5mg/d, every 1-2 weeks
10-0mg/d	:	decrease by 1-2.5 mg/d, every 1-4 weeks

Side Effects and its Management

Corticosteroid therapy produces both ocular and systemic side effects irrespective of the route of administration. Although, topical or periocular administration may result in significant systemic absorption, untoward systemic complications are for more likely after oral or parentral therapy, and their frequency is both dose and duration dependent.

Alternate day therapy produces less severe and fewer steroid – induced side effects and does not disturb the hypothalamo-pitutary axis.[40]

I. Systemic

1. Sodium and fluid retention
2. Hypertension
3. Osteoporosis
4. Peptic ulcer
5. Increased appetite
6. Poor wound healing

7. Acne
8. Increased sweating
9. Moodiness
10. Weight gain
11. Diabetes
12. Increased susceptibility to infections
13. Menstrual irregularity
14. Rarely thromboembolism

II. Ocular

1. Posterior subcapsular cataract
2. Glaucoma
3. Central serous retinopathy

Corticosteroid induced bone loss is a dose and duration dependent side effect.

Bone loss is inevitable during steroid therapy and commences within days of starting treatment. The rate of loss is greatest within the first 6 months during which time, typically 4-5% of bone is lost[35]. Eventually osteoporosis occurs in up to 50% of patients[36].

Trabecular bone is particularly affected, so effects are more marked in the spine and proximal femur. There is a 2.5-3 times increased risk of fracture compared with a control population.

Currently it is recommended that all patients should be given supplemental calcium (1000 / 1500 mg/d) and vitamin D (400 to 800 U/day) to retard bone loss[33].

Patients on long term corticosteroids ideally should be monitored with yearly bone density measurement and treated with biphosphonates (like etidronate or pamidronate) if bone loss is documented.

Patients on systemic corticosteroids, particularly those with a history of peptic ulcer disease or gastro esophageal reflux, benefit from prophylactic therapy with either an H_2 blocker (eg: Ranitidine, 150mg two to four times a day) or a proton pump inhibitor (e.g.: omeprazole, 20mg/d, half an hour before food).

Ideally, corticosteroids should be taken as a single dose in the morning. This is not only more physiologic, because the natural peak of adrenal corticosteroid production occurs in the morning, but also it allows the patient to sleep better.

Secondary open-angle glaucoma is most likely to occur after prolonged topical therapy with potent steroids. A more pronounced steroid-induced IOP increase is noted in patients with open angle glaucoma, diabetics and high myopes.

Posterior subcapsular cataract (PSCC) arise in a dose and duration dependent manner after long term oral corticosteroid therapy.

Children and patients with diabetes are more prone to develop. The mechanism of corticosteroid –induced cataract formation is believed to involve the binding of glucocorticoids to lens fibers, leading to biochemical alterations with protein aggregation in the cells and a change in refractive index.

Once established, the opacity is generally not reversible. However, regression of PSCC has been reported in children when therapy is discontinued.[37]

REVIEW OF LITERATURE

1. Unilateral Visual Impairment and Health related quality of life : the blue mountains eye study

E – M Chia, P Mitchell Rochtchina,S Foran,JJ Wan,JJ Wand

BJO 2003; 87: 392-395.

The study is aimed at determining the impairment of unilateral vision on health related quality of life (HRQOL) in an older community.

Study group, which includes 4433 eligible non –institutionalized permanent residents who was administered health survey questionnaire (SF36) in a door to door census. Study showed measurable impact on HRQOL in those patients who had moderate to severe non –correctable unilateral visual impairment caused by eye diseases like cataract.

2. Vision related quality of life in people with central retinal vein occlusion using the 25-item National Eye Institute Visual function questionnaire

Vincent A. Deramo, Terry A. Cox, Arjumand B. Syed, Paul P. Lee; Sheron Fekrat. Arch Ophthalmol. 2003; 121: 1297-1302.

Fifty one consecutive patients participated in this study. Forty eight patients had unilateral CRVO, and 5 had bilateral CRVO. All patients including reference group were administered NEIVFQ – 25 and analyzed result showed significantly decreased QOL when compared to reference group in patients with CRVO. This decrease in VFQ – 25 scores is related to the degree of visual loss in the better seeing eye and the overall systemic health of the patient.

3. Vision related quality of life in people with bilateral severe Age Related Macular Degeneration

Mark T. Cahill, Avie D. Banks; Saundra S. Stinnett, Cynthia A. Toth; Ophthalmology 2005; 112: 152-158.

Seventy patients with bilateral severe age related macular degeneration were administered NEI–VFQ–25 and SF – 12 questionnaires before macular translocation with 360^{o} peripheral retinectomy. According to this study, bilateral central vision loss due to ARMD had a profound impact on vision related QOL and had no relation with general health problems.

4. Vision functioning and General Health Status in Patients with Uveitis

M.Schitman, Gordon Jacobsen, Scolt M Whitcup. Arch Ophthalmol 2001; 119: 841-849.

This study conducted at the uveitis clinics at National Institute of health, Bethesda, enrolled seventy- six patients with uveitis over a period of 14 months and were administered NEI – VFQ – 25 and SF – 36

questionnaires to measure the visual functioning and quality of life in those patients. Results showed markedly poorer visual functioning and general health status than normal subjects. More severe the uveitis, poorer the quality of life.

5. Validity of the SF-12 quality of life instrument in patients with retinal diseases.

Devise R. Globe, Stainslav Levin; Tom S. Chang; Paul J. Mackenzie; Stanley Azen; Ophthalmology 2002; 109: 1793-1798.

As SF-36 questionnaire is too long and takes 12 minutes to complete, inclusion in clinical studies other then health outcome evaluation has been discouraged. Smaller version of this, SF-12 is being used widely to study health related quality of life in ophthalmic research, which is short and takes only 2 minutes. Above study was done to investigate the construct validity and reliability of the SF-12 with the SF-36 composite scores in patients with retinal diseases. The study gave the conclusion that SF-12 is a valid measure and the benefit of reduced administration time makes the SF-12 a recommended general quality of life outcomes tool.

6. Correlation between visual function and visual ability in patients with uveitis.

Gardiner AM, Armstrong RA, Danne MCM, Murray P; BJO; 2002; 86: 993-996.

The study compared the high (monocular and binocular) and low (binocular) contrast log MAR letter activities using a Bailey- Louis chart and contrast sensitivity with the vision related quality of life

answer using vision specific quality of life (VQOL) questionnaire in uveitis patients.

The study concluded that Binocular high contrast visual acuity is a good measure of how uveitis patients perform in real life situations. Vision related quality of life is worst in younger patients with poor binocular visual acuity.

7. Health related quality of life in patients with cataract and glaucoma

Lec BL., Wilson MR; J.Glaucoma 2000 Feb; 9(1): 87-94.

Increasing severity of glaucoma has been shown to be negatively related to vision targeted quality of life. The relationship between increasing severity of glaucoma and overall self perceived health status is inconclusive.

8. Quality of Life associated with visual loss. A time trade off utility analysis comparison with medical health status

Melissa M. Brom, Gary C. Brown, Sharma S, Busbee B. Ophthalmol 2003; 110: 1076-1081.

This paper presents a cross sectional utility value assessment to assess the visual utility values of patients with ocular disease and to

compare these values with those of patients with systemic health status. The conclusion is that visual loss is associated with a substantial and measurable diminution in quality of life.

9. The Madurai intraocular lens study III. Visual functioning and Quality of Life outcomes

Astrid Fletcher, V. Vijay Kumar, S. Selvaraj, R.D. Thulasiraj Leon B, Ellwein; Am. J. Ophthalmol. 1998; 125: 26-35.

It is a randomized control trial involving 3450 bilaterally vision impaired patients aged between 40 to 75 years of age with operable cataract. Patients were administered 31 item visual functioning questionnaire and 12 item quality of life questionnaire before and at 6 months and 12 months after surgery. Method of surgery was randomly assigned (either ECCE with IOL or ICCE). Conclusion of this study was that ECCE with IOL is better than ICCE and the visual functioning is better with highly significant P value ($P<0.0001$).

10. Treatment of uveitis with immunosuppressive agents.

Narsing A Rao; Buddi Rajeev; Indian journal of Ophthalmology; Oct 1998; 41(3):107-113.

This article has comprehensive details about principle of treating uveitis with steroids, various methods of administration and monitoring of its side-effects. It also includes indications and action of

commonly used immunosuppressives in uveitis with brief mention about its toxicity, precautions and monitoring for those toxicity.

AIM

To assess the vision and health related quality of life in patients with sight – threatening uveitis treated with immunosuppressive medication using 25 items National Eye Institute visual function questionnaire and short form 12 health survey.

Inclusion Criteria

1. Uveitis patient, started on immunosuppressive medication
2. Patient who knows Tamil
3. Willing to participate in study
4. Age > 18 years.

Exclusion Criteria

1. Patient either not willing to participate or who doesn't know Tamil.
2. Patient who cannot come for follow up
3. Who has hearing / speech difficulties
4. Age < 18 years

PATIENTS AND METHODOLOGY

Patient Selection

This study was conducted at uveitis clinic in a tertiary eye care centre in South India, which is a major referral centre for Ophthalmology.

All patients with sight – threatening uveitis who fit into inclusion criteria were enrolled over a period of six months from April 2004 to

October 2004. All patients were explained about the purpose of study and consent was obtained.

Data Collection

During the period of six months, 42 patients were enrolled and demographic data's were collected. The SF-12 and NEI – VFQ 25 questionnaires were applied by an interviewer and was made sure that only one person apply the questionnaire, the first time and also when the patients come back after six months. The questionnaires were completed before the ophthalmic examination to reduce the influence of the clinical encounter on patient's response.

All patients were requested to give their response for questions from the options given below each question. After responses were obtained, clinical data like visual acuity, onset, location of inflammation, laterality, level of inflammation, etiological diagnosis and type of immunosuppressive medication prescribed were recorded. Patients were explained about the importance of follow up and potential side effects of medication.

The enrolled patients were asked to review on a regular basis based on their uveitis status and the questionnaires were reapplied six months from the date of starting immunosuppressive medication. The patients who did not turn up for review, were telephoned and explained about importance of review and risk involved in having

medication without monitoring and were asked to come for follow up. Data of patients who did not turn up after six months were eliminated and patients who gave response prior and after six months of treatment were compared.

Statistical Methods

Original numeric values given as a response were recoded by following the scoring rules outlined for each of the questionnaires and these questions were grouped under their respective subscales in NEI-VFQ-25 and under PCS and MCS in health survey.

After grouping into sub-scales, the mean composite score, before and after treatment were calculated after averaging the scores of the respective subscale and by using the formula given below. Their significance is tested by using paired t-test value.

$$\text{Mean} = \frac{\text{Score for each items with a non missing answer}}{\text{Total number of items with non missing answers}}$$

RESULTS

42 patients were enrolled for this study over a period of six months and 35 patients came for follow up with follow up rate of 83.3%. The mean age of the patients were 36.8 years with females constituting 52.4% of total patients (table 1 & 2). Among these

patients, 64.3% of them are literate and 57.1% of them are unemployed (table 3 & 4). Diminished vision alone was a common compliant constituting 40.5%, and other complaints constituting the rest as shown in table 5.

Nearly 80% of them had uveitis in both eyes with acute onset constituting 54.8% of them (table 6 & 7). 61.9% of these patients had pan-uveitis ,16.7% of them had posterior uveitis, followed by anterior uveitis of 11.9% and intermediate uveitis of 9.5% (table 8). 78.6% of them had granulomatous uveitis with VKH syndrome being the most common etiological diagnosis (table 9 & 10).

71.4% of patients were treated with a combination of methotrexate and high dose oral corticosteroids and 26.2% of patients were given oral corticosteroids with a dose of 1mg / kg /day, which was considered as an immunosuppressive dose in this study. Only four patients (2.4%) were treated with Azathioprine and high dose oral corticosteroids (table 11).

Visual Function

The mean score of general health subscale showed slight dip in its value following treatment with a p value of 0.08, whereas other subscales like general vision, ocular pain, near activities, distance activities, mental health, social functioning, role difficulties,

dependency, colour vision and peripheral vision had significant increase in mean score following treatment with a significant p value.

Driving subscale had an improvement in its mean value following treatment, with p value of 0.066.

Health Status

Physical Composite Score (PCS)

General health question did not generate any mean value on both the occasions as only "POOR" option had a score of –2 with rest of all having a score of 0.

Bodily pain showed significant improvement following treatment with a p value of < 0.001. Rest of the components of PCS like physical functioning, role physical showed no significant change.

Overall physical composite score had a p value of 0.008.

Mental Composite Score (MCS)

Mental health, role emotional and social functioning subscale had significant rise in mean value following treatment, whereas vitality had no significant change, which is an emotional perception of having lot of energy or not.

Table – 1

	N	Minimum (in years)	Maximum (in years)	Mean (in years)	Standard Deviation
Age	43	14	69	36.81	14.681

Table – 2

Sex

	Frequency	Percent
Male	20	47.6
Female	22	52.4
Total	42	100.0

Table – 3

Educational Qualification

	Frequency	Percent
Literate	27	64.3
Illiterate	15	35.7
Total	42	100.0

Table – 4

Occupation

	Frequency	Percent
Employed	18	42.9
Unemployed	24	57.1
Total	42	100.0

Table – 5

Complaints

	Frequency	Percent
Diminished vision(DV)	17	40.5
DV+ Pain	12	28.5
DV +Redness	4	9.5
DV +Floaters	4	9.5
DV +Redness +Floaters	1	2.4
Pain + Redness	2	4.8
Pain +Redness+ Photophobia	1	2.4
Reduces + Floaters	1	2.4
Total	42	100.0

Table – 6

Laterality

	Frequency	Percent
Right Eye	4	9.5
Left Eye	5	11.9
Bilateral	33	78.6
Total	42	100.0

Table – 7

Onset

	Frequency	Percent

Acute	23	54.8
Chronic	19	45.2
Total	42	100.0

Table – 8

Location

	Frequency	Percent
Anterior	5	11.9
Intermediate	4	9.5
Posterior	7	16.7
Pan uveitis	26	61.9
Total	42	100.0

Table – 9

Severity

	Frequency	Percent
Granulomatous	33	78.6
Non granulomatous	7	16.7
Others	2	4.8
Total	42	100.0

Table – 10

Etiological Diagnosis

	Frequency	Percent	Valid Percent	Cumulative Percent
Bechet's syndrome	4	9.5	9.5	9.5

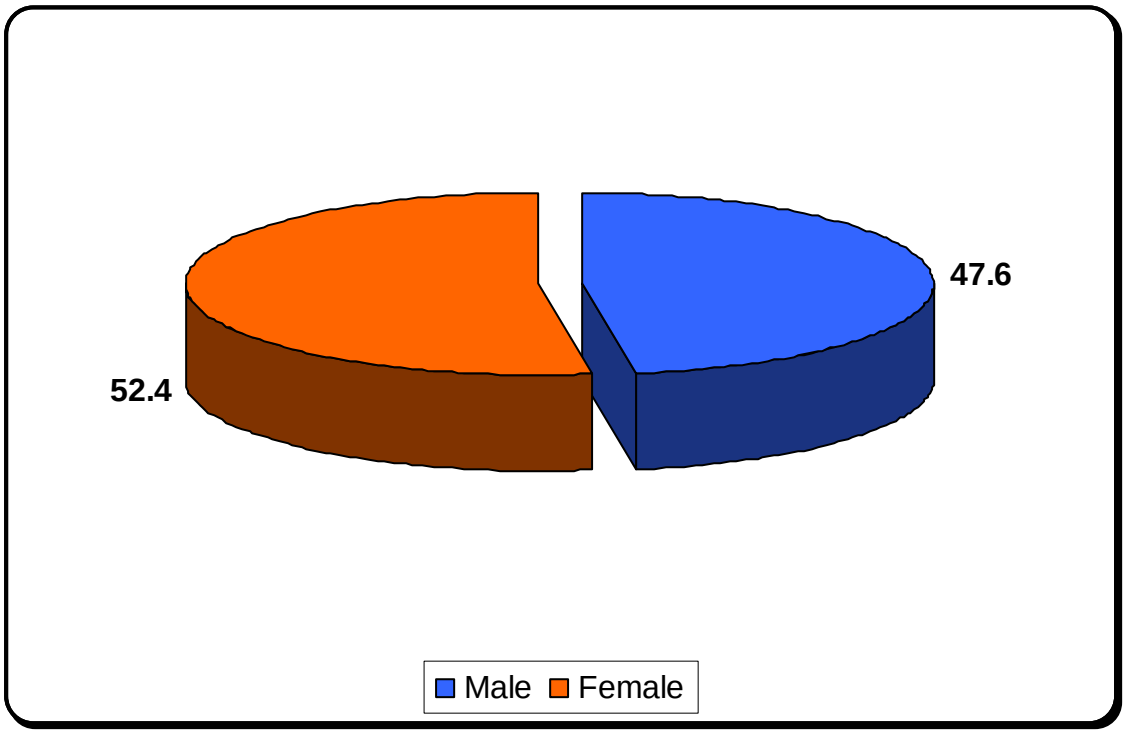
Diffuse scleritis	1	2.4	2.4	11.9
Endophthalmitis	1	2.4	2.4	14.3
GHPC	1	2.4	2.4	16.7
Leptospiral vasculitis	1	2.4	2.4	19.0
Nodular scleritis	1	2.4	2.4	21.4
Pars planitis	4	9.5	9.5	31.0
Posterior scleritis	1	2.4	2.4	33.3
Anterior scleritis	1	2.4	2.4	35.7
Retinal vasculitis	2	4.8	4.8	40.5
Rheumatoid sclero-uveitis	1	2.4	2.4	42.9
Sympathetic Ophthalmia	4	9.5	9.5	52.4
VKH syndrome	20	47.6	47.6	100.0
Total	42	100.0	100.0	

Table – 11

Treatment

	Frequency	**Percent**
High dose oral Corticosteroids	11	26.2
Azathioprine + High dose oral Corticosteroids	1	2.4
Methotrexate+ High dose oral Corticosteroids	30	71.4
Total	42	100.0

GENDER



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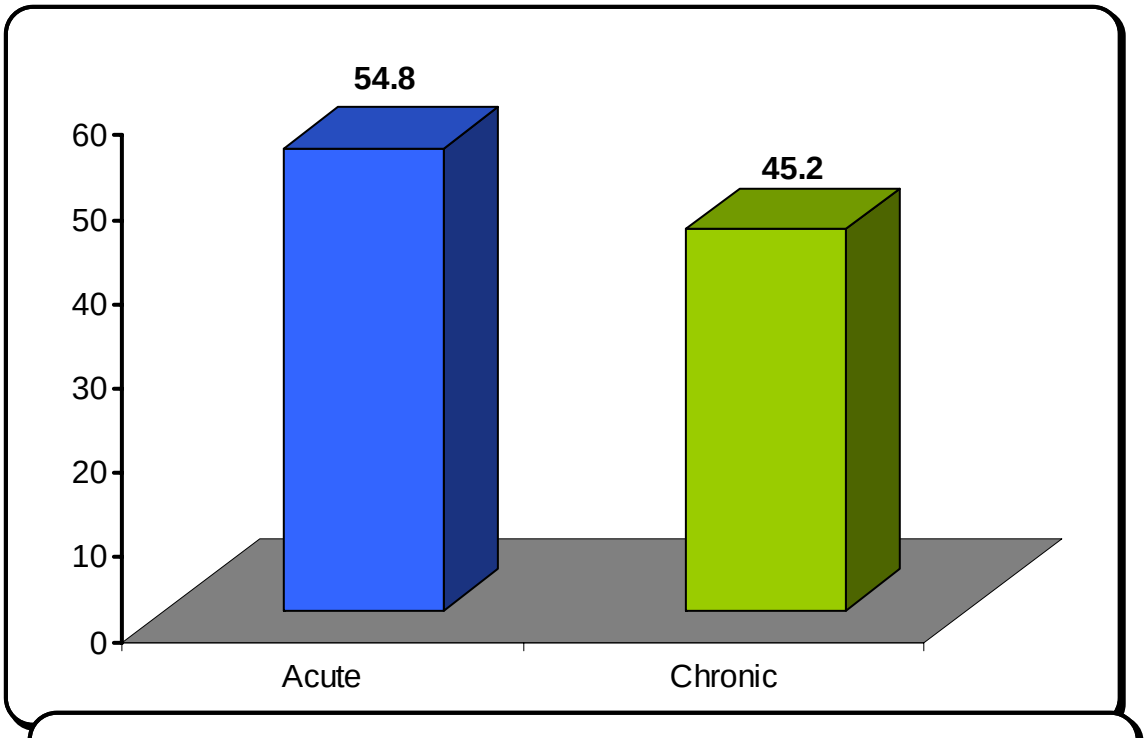
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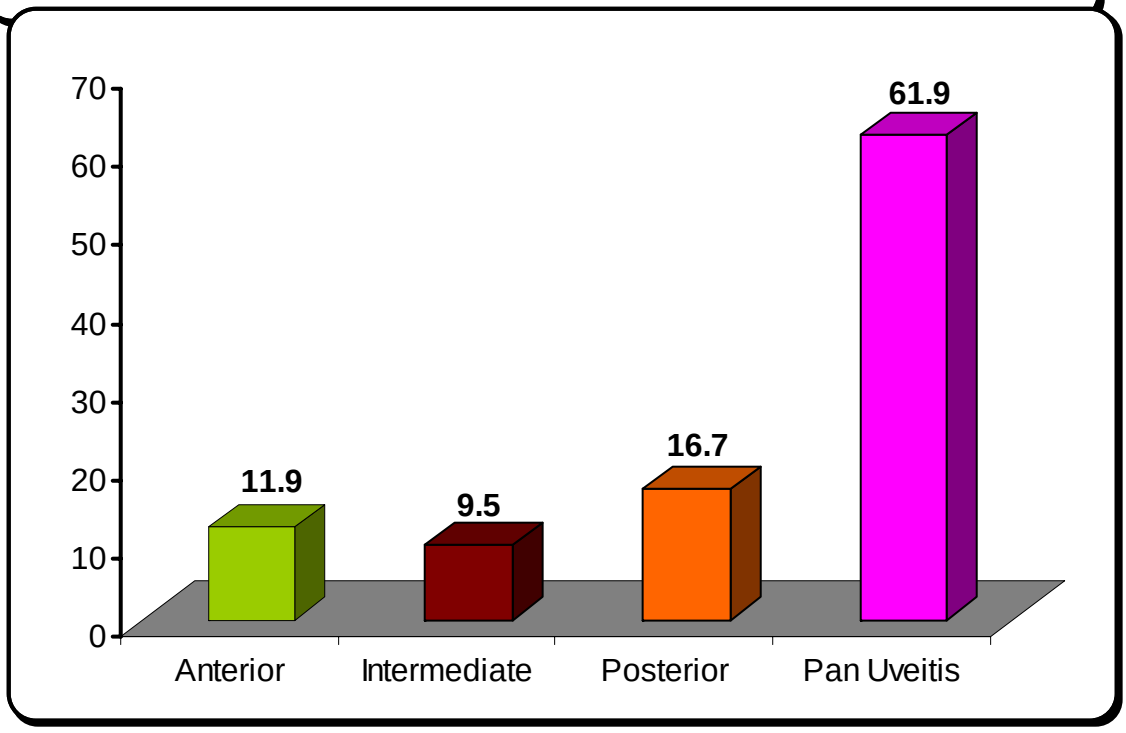
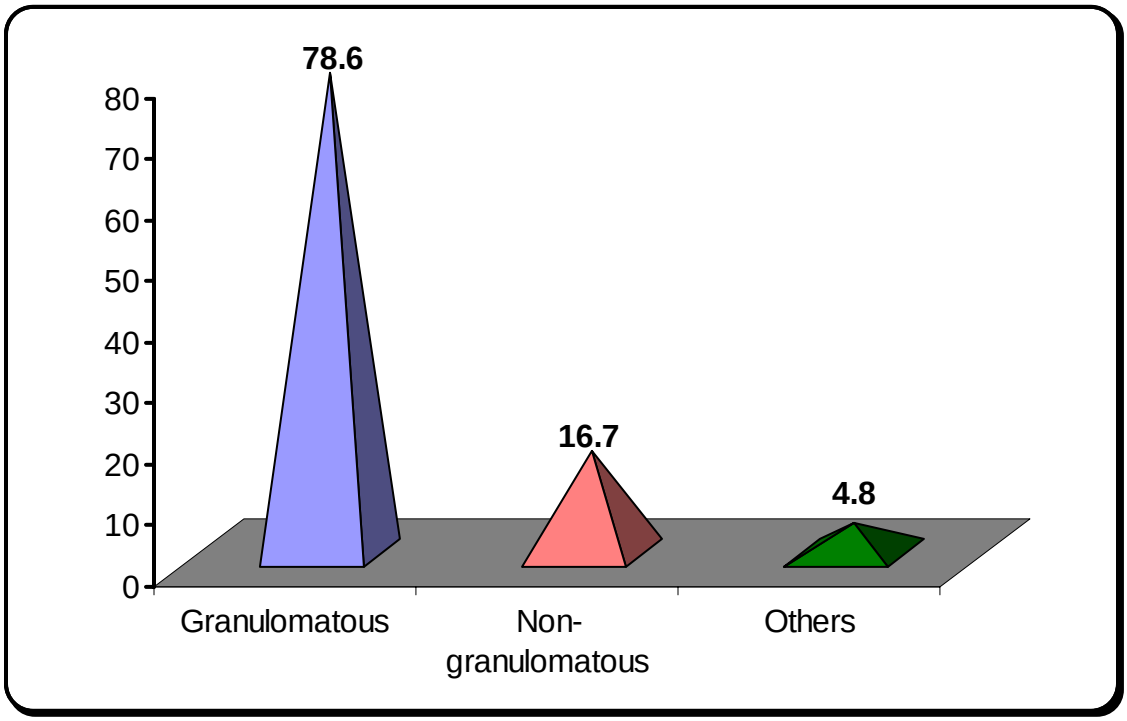
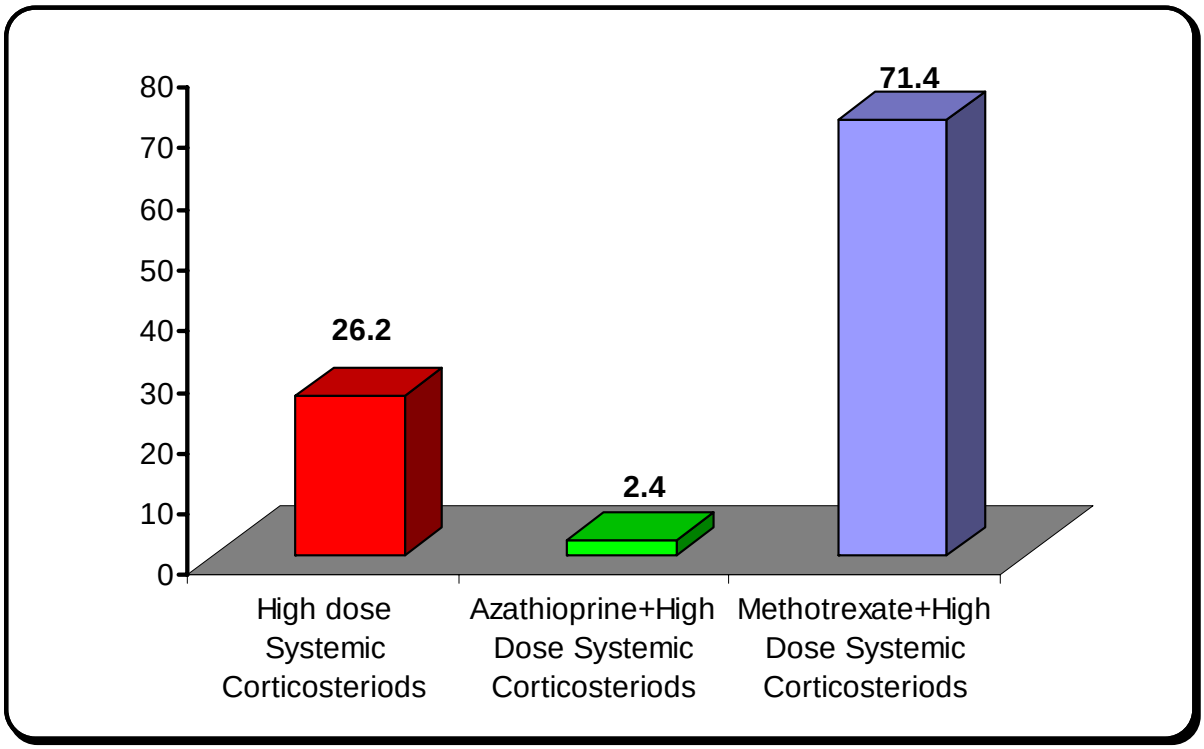
45.2
60
50
40
30
20
10
0
Acute
Chronic


70
60
50
40
30
20
10
0
11.9
9.5
16.7
61.9
Anterior
Intermediate
Posterior
Pan Uveitis

SEVERITY


78.6
16.7
4.8
80
70
60
50
40
30
20
10
0
Granulomatous
Non-granulomatous
Others


71.4
26.2
2.4
80
70
60
50
40
30
20
10
0
High dose Systemic Corticosteriods
Azathioprine+High Dose Systemic Corticosteriods
Methotrexate+High Dose Systemic Corticosteriods

VISUAL FUNCTION AND QUALITY OF LIFE

Descriptive Statistics

General Health	N	Minimum	Maximum	Mean	Std. Deviation	P Value
Pre-treatment	35	.00	100.00	94.2857	18.27659	0.087
Post-treatment	35	50.00	100.00	89.2857	15.20172	

General Vision	N	Minimum	Maximum	Mean	Std. Deviation	P Value
Pre-treatment	35	.00	100.00	28.5714	30.40345	0.000
Post-treatment	35	.00	100.00	68.5714	30.52413	

Ocular Pain	N	Minimum	Maximum	Mean	Std. Deviation	P Value
Pre-treatment	35	12.50	100.00	60.3571	30.08653	.000
Post-treatment	35	12.50	100.00	90.7143	19.25612	

Near Activities	N	Minimum	Maximum	Mean	Std. Deviation	P Value
Pre-treatment	33	.00	100.00	47.9798	29.31734	0.000
Post-treatment	31	8.33	100.00	89.2473	23.68715	

Distance Activities	N	Minimum	Maximum	Mean	Std. Deviation	P Value
Pre-treatment	32	.00	100.00	50.2604	32.41230	0.000
Post-treatment	32	25.00	100.00	93.2292	15.32759	

Mental Health	N	Minimum	Maximum	Mean	Std. Deviation	P Value
Pre-treatment	35	.00	68.75	33.5714	23.68246	0.000
Post-treatment	35	18.75	100.00	82.8571	24.17494	

Social Functioning	N	Minimum	Maximum	Mean	Std. Deviation	P Value
Pre-treatment	33	.00	100.00	46.5909	31.75725	0.000
Post-treatment	34	25.00	100.00	93.7500	16.06391	

Role Difficulties	N	Minimum	Maximum	Mean	Std. Deviation	P Value

Pre-treatment	35	.00	100.00	44.2857	36.67510	0.000
Post-treatment	35	.00	100.00	80.0000	29.73535	

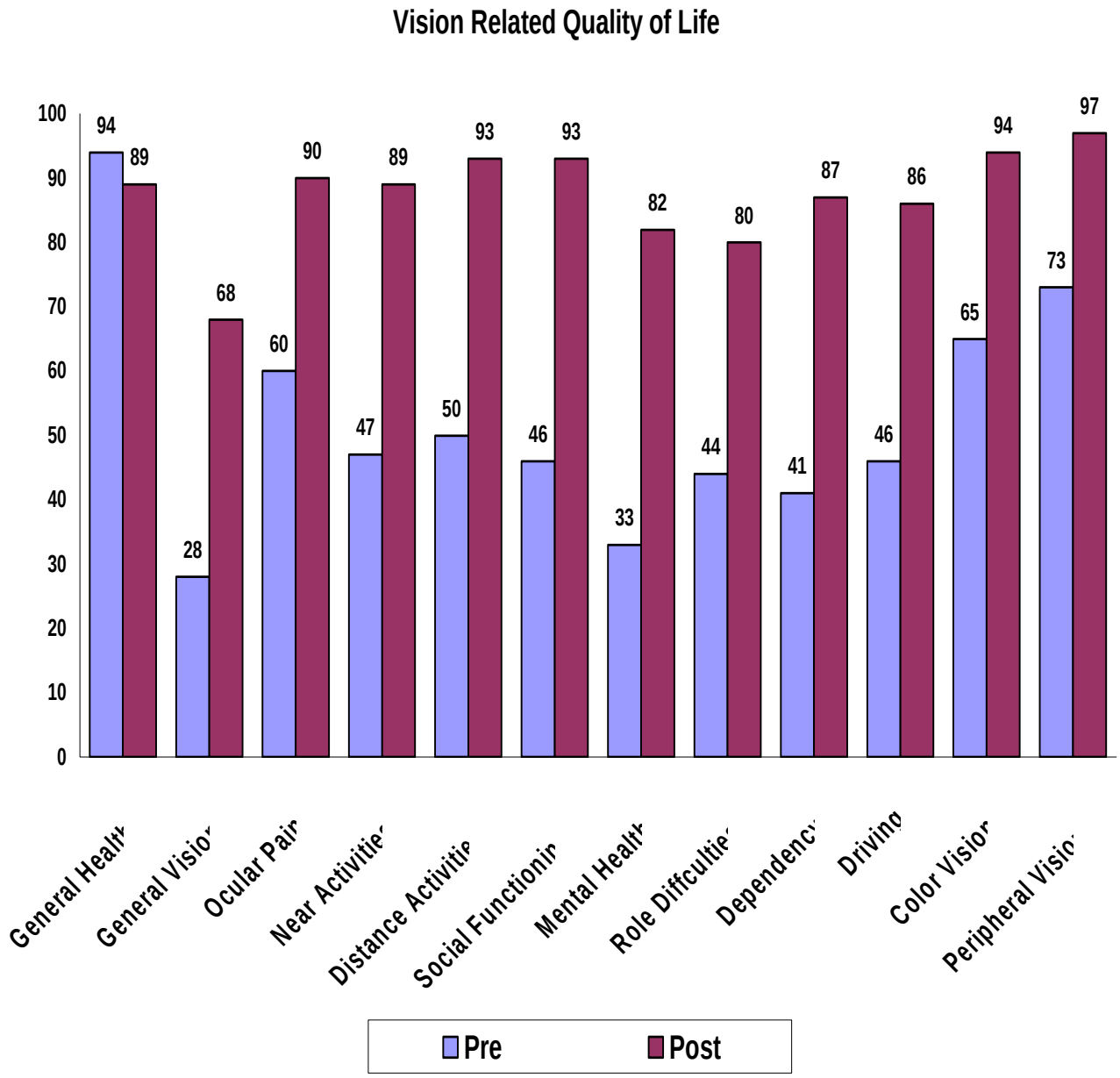
Dependency	N	Minimum	Maximum	Mean	Std. Deviation	P Value
Pre-treatment	35	.00	100.00	41.6667	40.62421	0.000
Post-treatment	35	16.67	100.00	87.8571	23.94360	

Driving	N	Minimum	Maximum	Mean	Std. Deviation	P Value
Pre-treatment	5	16.67	75.00	46.6667	20.91650	0.066
Post-treatment	5	16.67	100.00	86.1111	34.02069	

Colour Vision	N	Minimum	Maximum	Mean	Std. Deviation	P Value
Pre-treatment	35	.00	100.00	65.7143	33.25797	0.000
Post-treatment	35	50.00	100.00	68.5714	14.95792	

Peripheral Vision	N	Minimum	Maximum	Mean	Std. Deviation	P Value
Pre-treatment	35	.00	100.00	73.5714	33.72840	.001

Post-treatment	35	75.00	100.00	97.1429	8.07007	



SF-12 HEALTH SURVEY

Descriptive Statistics

Physical composite score:

General Health	N	Minimum	Maximum	Mean	Std. Deviation	P Value
Pre-treatment	35	.00	.00	.0000	0.00000	1.000
Post-treatment	35	.00	.00	.0000	0.00000	

Bodily Pain	N	Minimum	Maximum	Mean	Std. Deviation	P Value
Pre-treatment	35	.00	2.00	.8000	.71948	.000
Post-treatment	35	.00	1.00	.2000	.40584	

Physical Functioning	N	Minimum	Maximum	Mean	Std. Deviation	P Value
Pre-treatment	35	.00	3.50	.2571	.72123	0.056
Post-treatment	35	.00	1.00	.0286	.16903	

Role Physical	N	Minimum	Maximum	Mean	Std. Deviation	P Value
Pre-treatment	35	.00	1.50	1.3714	.42604	.083
Post-treatment	35	1.50	1.50	1.5000	.00000	

Overall PCS score	N	Minimum	Maximum	Mean	Std. Deviation	P Value
Pre-treatment	35	.00	1.83	.6782	.29133	.008
Post-treatment	35	.50	.83	.5429	.8424	

Mental composite score

Mental Health	N	Minimum	Maximum	Mean	Std. Deviation	P Value
Pre-treatment	35	-10.50	.00	-7.6000	2.70566	.000
Post-treatment	35	-10.50	.00	-2.2571	2.77958	

Vitality	N	Minimum	Maximum	Mean	Std. Deviation	P Value
Pre-treatment	35	-5.00	.00	-.8286	.85700	.371
Post-treatment	35	-1.00	.00	-.6286	.49024	

Role Emotional	N	Minimum	Maximum	Mean	Std. Deviation	P Value
Pre-treatment	35	-6.50	.00	-1.2143	2.50965	.000
Post-treatment	35	-6.50	.00	-5.2000	2.63796	

Social Functioning	N	Minimum	Maximum	Mean	Std. Deviation	P Value
Pre-treatment	35	-6.00	.00	-6.7714	2.05921	.000
Post-treatment	35	-8.00	.00	-2.0000	2.65684	

Overall MCS Scores	N	Minimum	Maximum	Mean	Std. Deviation	P Value
Pre-treatment	35	-6.83	-1.33	-4.2048	1.12102	.000
Post-treatment	35	-5.00	-1.33	-2.9238	.82282	

DISCUSSION

Uveitis is a major cause of ocular morbidity and is reportedly responsible for an estimated 30,000 new cases of legal blindness

annually in the United States.[41] It's high prevalence in India was highlighted by Dandona et al[42] and it warranted an immediate and effective management. High dose oral corticosteroids and cytotoxic medications are being used as a final rung in management inspite of its documented potential side effects. Henceforth, it was decided to assess vision related quality of life in immunosuppressive treated uveitic patients and to know the impact of its side effects on their health status.

General health of these patients on immunosuppressive medication showed slight decrease in mean score after six months due to the side effects like gastritis, weight gain, emotional influence on taking too many pills etc, whereas *bodily pain* showed significant improvement with a p value of <0.001, as their ocular pain interfering with daily activities showed improvement with medication. Treatment had no influence on physical functioning and vitality and it didn't cause any physical morbidity.

Visual functions like near and distance activities, role difficulties pertaining to vision showed marked improvement with a p value of <0.001. It almost eliminated the dependency of these patients, as most of them had an attender during their first visit. Emotional disturbance experienced by these patients due to defective vision showed

significant relief with treatment, as indicated by rise in post treatment mean scores of *mental health* and *MCS*.

Social functioning like visiting people in their homes or attending marriages which was influenced by defective vision and ocular pain, showed significant change after six months of treatment. As 53% of patients in this study are females and more than half of the males had no experience of driving, *driving* subscale questions were answered only by 14% of them (only 5 patients) and had moderate effect with a p value of < 0.066, even though, the mean value had a significant improvement .

Overall, the visual function, vision related quality of life and mental health of these patients improved significantly, following treatment of sight–threatening uveitis with immunosuppressive medication, with slight dip in general health status due to its side effects.

CONCLUSION

Vision and health related quality of life in forty two uveitic patients, who were on immunosuppressive medication were evaluated prior to and six months following treatment showed significant improvement in:

- *Visual function and vision related quality of life* .
- *Mental health* .
- *Social functioning*
- *Ocular pain*.

Treatment almost eliminated the *dependency* and *role difficulties* in these patients. Study showed the *general health status* was affected due to its side effects and medication had no influence on *physical functioning*. The influence of potential side effects of medication on health status in these patients on prolonged course needs to be assessed.

So, judicious use of high dose oral corticosteroids and any cytotoxic medication as a final step in management of sight threatening uveitis is important and it does improve the quality of life significantly in uveitic patients, even though it has a mild impact on general health status of these patients due to its side effects.

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ANNEXURE

Table 1

Averaging of Items to Generate VFQ – 25 sub-scales

Scale	Number of Items	Items to be averaged
1. General health	1	1

2. General vision	1	2
3. Ocular pain	2	4, 19
4. Near activities	3	5, 6, 7
5. Distance activities	3	8, 9, 14
6. Social functioning	2	11, 13
7. Mental health	4	3, 21, 22, 25
8. Role Difficulties	2	17, 18
9. Dependency	3	20, 23, 24
10.Driving	3	15c, 16, 16a
11.Colour vision	1	12
12.Peripheral vision	1	10

Table 2

Scoring key: Recoding of items

Item Numbers	Precoded choices	To recoded value of:
1, 3, 4, 15c, 2	1	100
	2	75
	3	50
	4	25
	5	0

5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 16,16a	1	100
	2	75
	3	50
	4	25
	5	0
	6	*
17, 18, 19, 20, 21, 22, 23, 24, 25	1	0
	2	25
	3	50
	4	75
	5	100

Table 3

Averaging of items to generate SF-12 subscales

Physical Composite Score (PCS)	**Questions**
1. General health	1
2. Bodily pain	8
3. Physical function	2, 3
4. Role – physical	4, 5

Mental Composite Score	**Questions**

(MCS)	
1. Mental health	9,11
2. Vitality	10
3. Role emotional	6,7
4. Social functioning	12

PROFORMA

Name : DATE :

Age : Presentation :_____

Sex : ☐ Male ☐ Female Start of immuno suppressives _____

1st Follow up _____

2nd Follow up_____

Educational Qualification : Literate ☐ Illiterate ☐

Occupation : Employed ☐ Unemployed ☐

Income :

Personal History : DM ☐ SHT ☐ Cardiac ☐
Asthma ☐ Any allergy ☐
Other _____

Complaints : Pain ☐ Photophobia ☐ DV ☐
Redness ☐ Floaters ☐

Duration :

Laterality : RE ☐ LE ☐ Bilateral ☐

Diagnosis : Acute ☐ Chronic ☐
Anterior ☐ Intermediate ☐ Posterior ☐ Pan ☐
uveitis Granulomatous ☐
nongranulomatous ☐

Etiological / Specific Diagnosis : _____

Treatment : Cyclophosphamide ☐ Chlorambucil ☐
Azathioprine ☐ Cyclosporine A ☐
Methotrexate ☐ Corticosteriods *Local ☐
others ☐ *Systemic ☐

Dosage : _____

Examination	**First Visit**		**6th month**	
	RE	LE	RE	LE
1. Visual acuity	☐	☐	☐	☐
2. Band keratopathy	☐	☐	☐	☐
3. KP's (G/N)	☐	☐	☐	☐
4. Anterior chamber				

Cells	☐ ☐	☐ ☐
Flare	☐ ☐	☐ ☐
5. Iris atrophy	☐ ☐	☐ ☐
6. Posterior synechiae	☐ ☐	☐ ☐
7. NVI	☐ ☐	☐ ☐
8. Iris nodules (K/B)	☐ ☐	☐ ☐
9. Cataract	_____	_____
10. AVF Cells	☐ ☐	☐ ☐
11. Vitreous opacities (E/H)	☐ ☐	☐ ☐
12. Vasculitis	☐ ☐	☐ ☐
13. Granuloma	☐ ☐	☐ ☐
14. Exudative RD	☐ ☐	☐ ☐
15. Retinitis	☐ ☐	☐ ☐
16. Choroiditis	☐ ☐	☐ ☐
17. IOP	☐ ☐	☐ ☐

Investigations

18. Hemoglobin %	_____	_____
TC	_____	_____
DC	_____	_____
ESR	_____	_____
Platelet count	_____	_____
Peripheral smear	_____	_____
Bleeding time	_____	_____
Clotting time	_____	_____
Mantoux	_____	_____
VDRL	_____	_____

Blood Urea _____ _____

S. Creatinine _____ _____

Liver function test

* SGOT _____ _____

* SGPT _____ _____

* Serum Bilirubin _____ _____

Urine

*Albumin _____ _____

* RBC's _____ _____

Systemic Side effects

Headache	☐	☐
Increased appetite	☐	☐
Weight gain	☐	☐
Fever	☐	☐
Poor wound healing	☐	☐
Increased sweating	☐	☐
Arthritis	☐	☐
Gingival hyperplasia	☐	☐
Alopecia	☐	☐
Hirsuitism	☐	☐
Pedal edema	☐	☐
Menstrual irregularity	☐	☐
Acne	☐	☐
Diarrhea	☐	☐

Ulcerative stomatitis	☐	☐
Nausea	☐	☐
Vomiting	☐	☐
Epigastric pain	☐	☐
Hematuria	☐	☐
Postural Hypotension	☐	☐
Moodiness	☐	☐
Insomnia	☐	☐

VISUAL FUNCTIONING QUESTIONNAIRE –25

PART – I

General Health and Vision

1. In general, would you say your **overall health** is?

   1. Excellent 2. Very Good 3. Good
   4. Fair 5. Poor ☐

2. At the present time, **would you say your eyesight** using both eyes (with glasses or contact lenses, it you wear them)

   1. Excellent 2. Very Good 3. Good
   4. Fair 5. Poor ☐

3. How much of the time do you **worry** about your eyesight?

   1. None of the time 2. A little of the time 3. Some of the time
   4. Most of the time 5. All of the time ☐

4. How much **pain or discomfort** have you had **in and around your eyes**? would you say it is?

   1. None 2. Mild 3. Moderate
   4. Severe 5. Very Severe ☐

PART - II

Difficulty with Activities

5.	How much difficulty do you have **reading ordinary**	1	2	3	4	5	6

	print in newspapers?						
6.	How much difficulty do you have doing work or hobbies that require you **to see well up close**, such as looking, sewing, fixing things around the house of using hand tools?	1	2	3	4	5	6
7.	Because of your eyesight, how much difficulty do your have finding something on a **crowded shelf**?	1	2	3	4	5	6
8.	How much difficulty do you have **reading street signs or the names of stores?**	1	2	3	4	5	6
9.	Because of your eyesight, how much difficulty do you have **going down steps, stairs, or curbs in dim light or at night?**	1	2	3	4	5	6
10.	How much difficulty do you have **noticing objects off to the side while you are walking along?**	1	2	3	4	5	6
11.	How much difficulty do you have **seeing how people react to things your say?**	1	2	3	4	5	6
12.	How much difficulty do you have **picking out and matching you own clothes?**	1	2	3	4	5	6
13.	How much difficulty do you have **visiting with people in their homes, at parties, or in restaurants?**	1	2	3	4	5	6
14.	How much difficulty, do you have **going out to see movies, plays or sports events?**	1	2	3	4	5	6

Note :

1. No difficulty at all
2. A little difficulty
3. Moderate difficulty
4. Extreme difficulty
5. Stopped doing this because of your eyesight
6. Stopped doing this for other reasons or not interested in doing this

15. **Now I'd like to ask about driving a car.** Are you currently driving, at least once in a while?
    1) Yes (Skip to Q15c) 2) No ☐

15a. **If No, Ask :** Have you never driven a care or have you given up driving?
    1) Never drove (Skip to Q 17) 2) Gave up ☐

15b. **If gave up driving :** was that mainly because of your eyesight, mainly for some other reason, or because of both your eyesight and other reasons?
    1) Mainly eyesight 2) Mainly other reasons ☐
    3) Both eyesight and other reasons

15c. If currently driving : how much difficulty do you have driving the daytime in familiar places?

1) No difficultly at all 2) A little difficultly
3) Moderate difficulty 4) Extreme difficulty ☐

16. How much difficulty do you have **driving at night?**

1) No difficulty at all 2) A little difficulty
3) Moderate difficulty 4) Extreme difficulty
5) Have you stopped doing this because of your eyesight ☐
6) Have you stopped doing this for other reasons or are you not interested in doing this .....

16a. How much difficulty do you have **driving in difficult conditions,** such as in bad weather, during rush hour, on the freeway, or in city traffic?

1) No difficult at all 2) A little difficulty
2) Moderate difficulty 4) Extreme difficulty
5) Have you stopped doing this because of your eyesight?
6) Have you stopped doing this for other reasons or are you not interested
in doing this .....

17. Do you accomplish less than you would like because of your vision?

1) All of the time 2) Most of the time 3) Some of the time
4) A little of the time 5) None of the time

18. Are you limited in how long you can work or do other activities because of your vision?

1) All of the time 2) Most of the time 3) Some of the time
4) A little of the time 5) None of the time

19. How much does pain or discomfort in or around your eyes, for example, burning , itching, or aching, keep you from doing what you'd like to be doing?

1) All of the time 2) Most of the time 3) Some of the time
4) A little of the time 5) None of the time

20.	**I stay home most of the time** because of my eyesight	1	2	3	4	5
21.	I feel **frustrated** a lot of the time because of my eyesight	1	2	3	4	5
22.	I have much less control over what I do, because of my eyesight	1	2	3	4	5
23.	Because of my eyesight, I have to **rely too much on what other people tell me**	1	2	3	4	5
24.	**I need a lot of help** from others because of my eyesight	1	2	3	4	5

25.	I worry about **doing things that will embarrass myself** or others, because of my eyesight.	1	2	3	4	5

Note:

1. Definitely true
2. Mostly true
3. Not true
4. Mostly false
5. Definitely false

SF 12 HEALTH SURVEY

1. In general, would you say your health is,

   Excellent ☐ (0) Very good ☐ (0) Good ☐ (0)
   Fair ☐ (0) Poor ☐ (-2)

2. Does your health now, limit you in activities like moving a table, pushing a vaccum cleaner or playing?
   Yes limited a lot ☐ (4) Yes limited a little ☐ (2)
   No, non limited at all ☐ (0)

3. Does you health now limit you in climbing several flights of stairs?
   Yes limited a lot ☐ (4) Yes limited a little ☐ (2)
   No, non limited at all ☐ (0)

During past 4 weeks have you had any problem as a result of your **physical health?**

4. Accomplished less than you would like? Yes ☐ (1) No ☐ (0)
5. Were limited in the kind of work or other activities? Yes ☐ (2) No ☐ (0)

During past 4 weeks have you had any problems as a result of emotional problems (feeling depressed or anxious)

6. Accomplished less than you would like? Yes ☐ (7) No ☐ (0)
7. Didn't do work or other activities as carefully as usual? Yes ☐ (6) No ☐ (0)
8. During the past 4 weeks, how much did pain interfere with your normal work (both working outside or housework)?
   Not at all ☐ (0) A little bit ☐ (1) Moderately ☐ (1)
   Quite a bit ☐ (2) Extremely ☐ (1)

9.	How much of the time during the past 4 weeks	1 (0)	2	3	4	5 (-	6

	have you felt calm and peaceful?		(-2)	(-4)	(-6)	10)	(-10)
10.	How much of the time during the past 4 weeks did you have a lot of energy?	1 (0)	2 (-1)	3 (-2)	4 (-3)	5 (-5)	6 (-6)
11.	How much of the time during the past 4 weeks have you felt downhearted and blue?	1 (-16)	2 (-11)	3 (-8)	4 (-5)	5 (-2)	6 (-0)
12.	During the past 4 weeks, how much of the time has your physical health or emotional problem interfered with your social activities (like visiting friends, relatives etc.,)	1 (-6)	2 (-8)	*	4 (-6)	5 (-3)	6 (0)

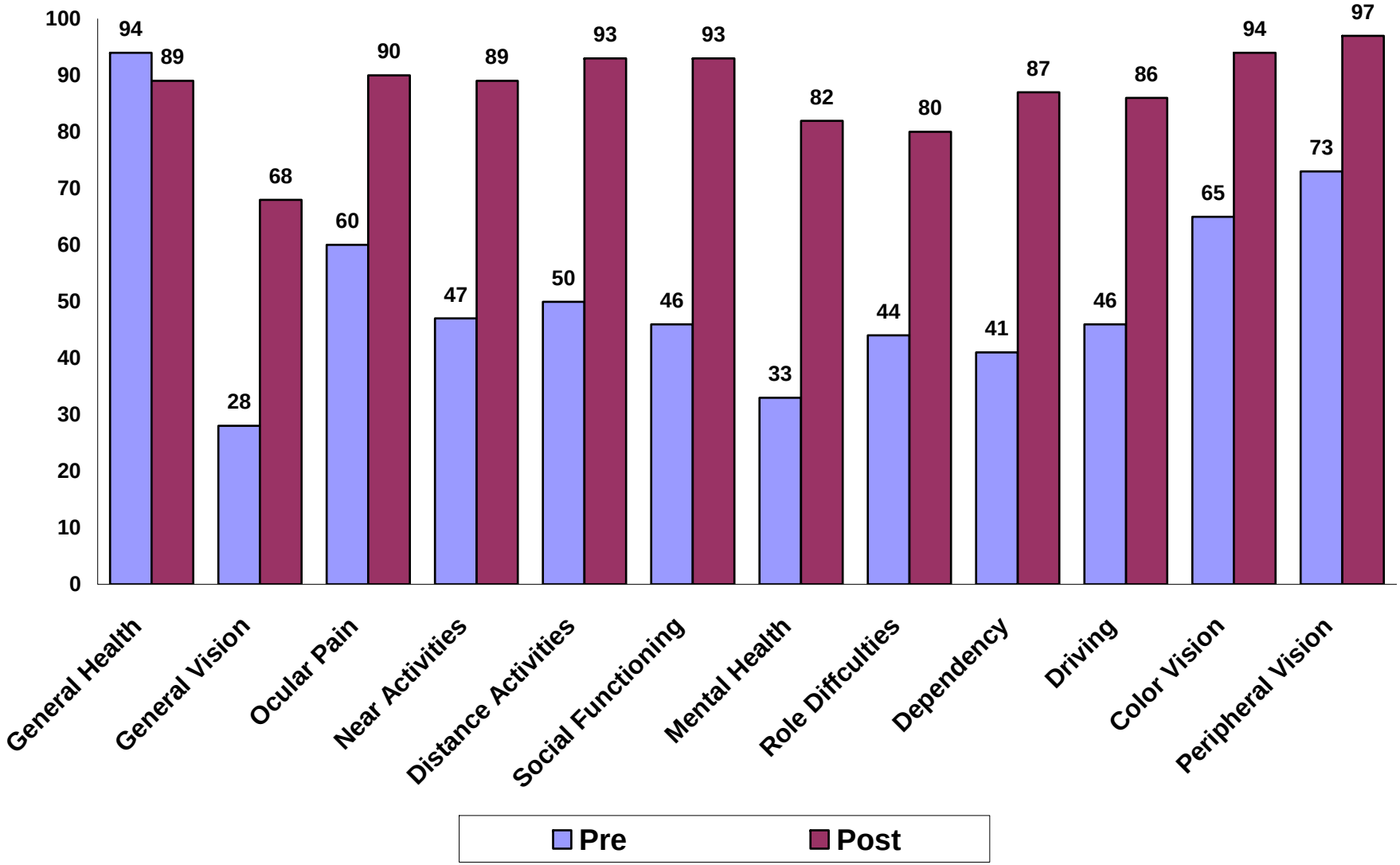
Note

1. All of the time
2. Most of the time
3. A good bit of the time
4. Some of the time
5. A little of the time
6. None of the time

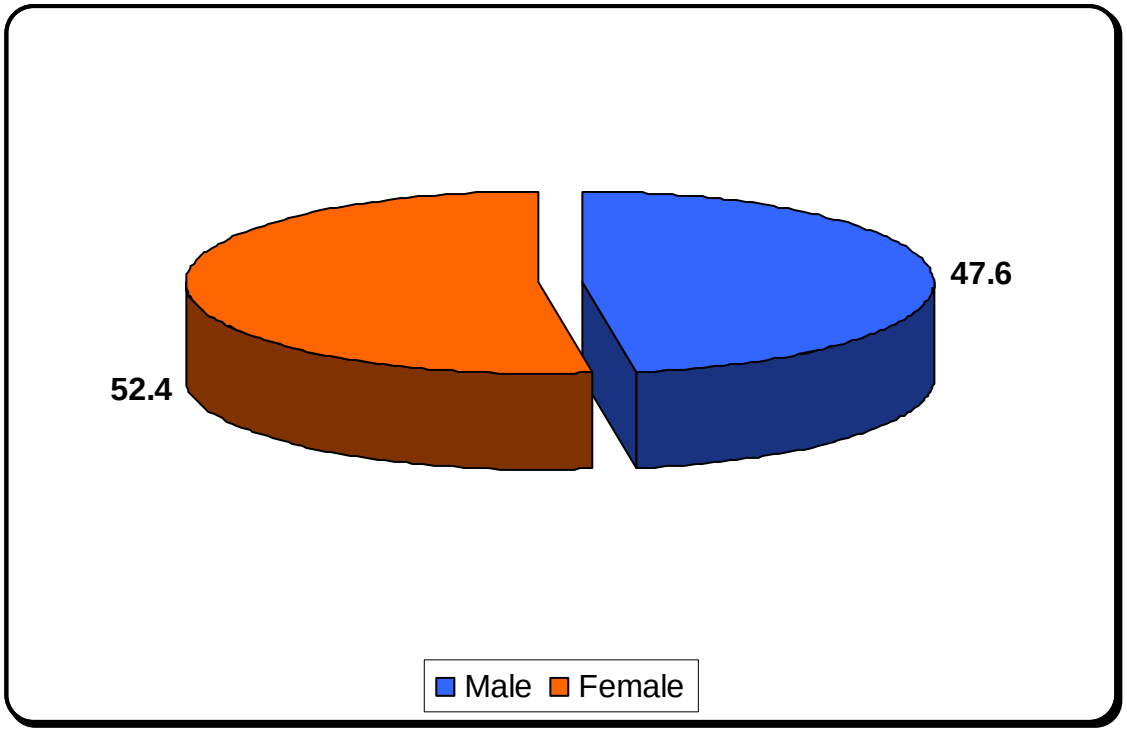
CLINICALLY USEFUL IMMUNOSUPPRESSIVE AGENTS[32]

Generic Name (Class)	Mechanism of Action	Dosage	Toxicity	Precautions
1. Cyclophosphamide (Alkylating agent)	Miscoding and blocking of DNA replication	1-2 mg / kg / d	1. Sterile hemorrhagic cystitis 2. Alopecia 3. Anemia 4. Thrombocytopenia	❖ Blood counts (2 weekly) ❖ Urine analysis (2 weekly) ❖ Morning dosage ❖ 2-3 liters of fluid /day ❖ Frequent voiding
2. Chlorambucil (Alkylating agent)	Miscoding and blocking of DNA replication	0.1 mg/ kg/d Max dose : 18 mg / d	1. Reversible bone marrow Suppression 2. Leucopenia 3. Azoospermia 4. Leukemia's	❖ Blood counts (1-2 weekly)
3. Methotrexate (Folic acid antagonist)	Inhibits the production of tetrahydrofolate (THF) thereby reducing synthesis of DNA. Enzyme inhibited is dihydrofolate reductase	Single low dose pulsed therapy PO:7.5 - 12.5 mg/wk Max : 25 mg/wk	1. Nausea 2. Malaise / alopecia 3. Ulcerative stomatitis 4. Pancytopenia 5. Hepatotoxicity	❖ Blood counts (2wkly) ❖ LFT mainly SGOT & SGPT (4 wkly) ❖ Liver biopsy after 1.5 gm cumulative dose ❖ Folinic acid 1 mg/d

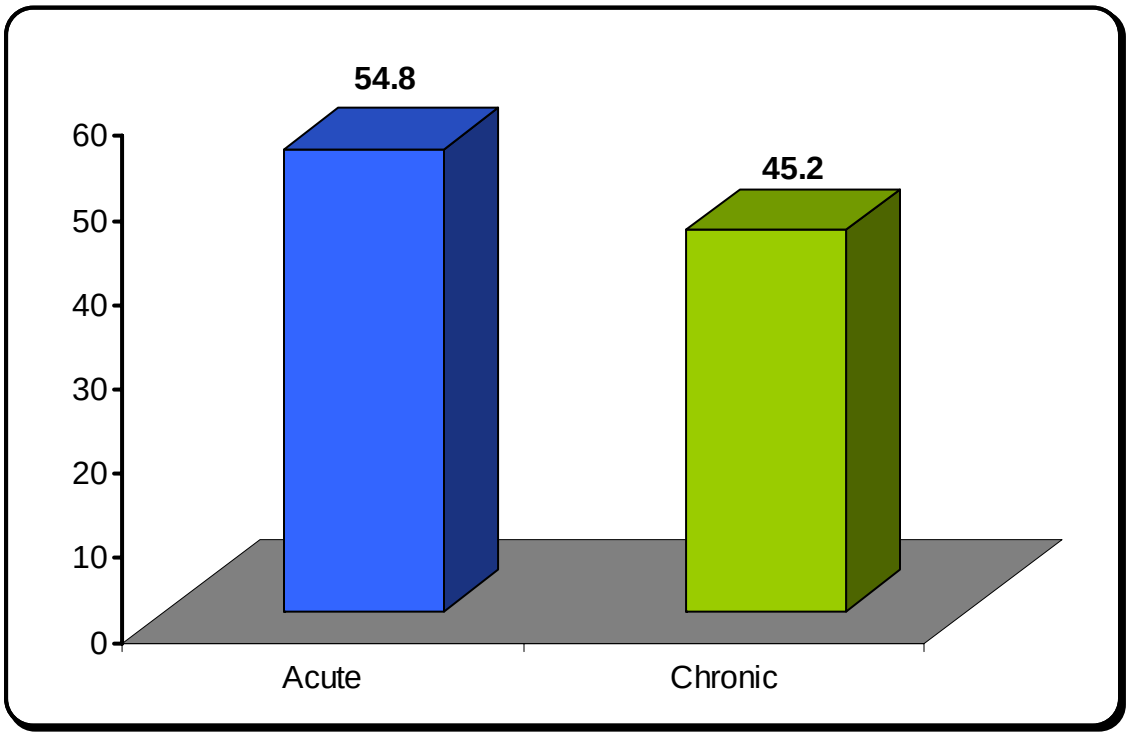
4. Azathioprine (purine antagonist)	Interferes with synthesis of purine bases and therefore RNA and DNA synthesis	PO : 1-2.5 mg / kg / d in one or more doses	1. Myelosuppresion 2. GI distress 3. Secondary infections	❖ Blood count (1-2 wkly)
5. Cyclosporine A (Macrolide)	Inhibits transcription of IL-2 and IL-4 in T cells thus suppressing activation and proliferation of T cells	PO : 5-7 mg / kg/d	1. Nephrotoxic 2. Gingival hyperplasia 3. Nausea & Vomiting 4. Hypertrichosis 5. Systemic hypertension 6. Mild anemia	❖ Renal functions (4wkly) ❖ Blood count (4 wkly) ❖ Monitor serum level (150-200 ng/ml)
6. FK – 506 (Macrolide)	Prevents transcription of IL-2 and IL-4 genes leading to inhibition of T-helper cell proliferation and activation	PO: 0.1 to 0.15 mg/ kg/d in two divided doses.	1. Renal impairment 2. Tremors 3. Hyperglycemia	❖ Serum creatinine (2wkly) ❖ Blood count (2 wkly) ❖ Maintain blood level below 20ng/ml


Vision Related Quality of Life
100
90
80
70
60
50
40
30
20
10
0
94
89
28
68
60
90
47
89
50
93
46
93
33
82
44
80
41
87
46
86
65
94
73
97
General Health
General Vision
Ocular Pain
Near Activities
Distance Activities
Social Functioning
Mental Health
Role Diffculties
Dependency
Driving
Color Vision
Peripheral Vision
Pre
Post

GENDER



ONSET



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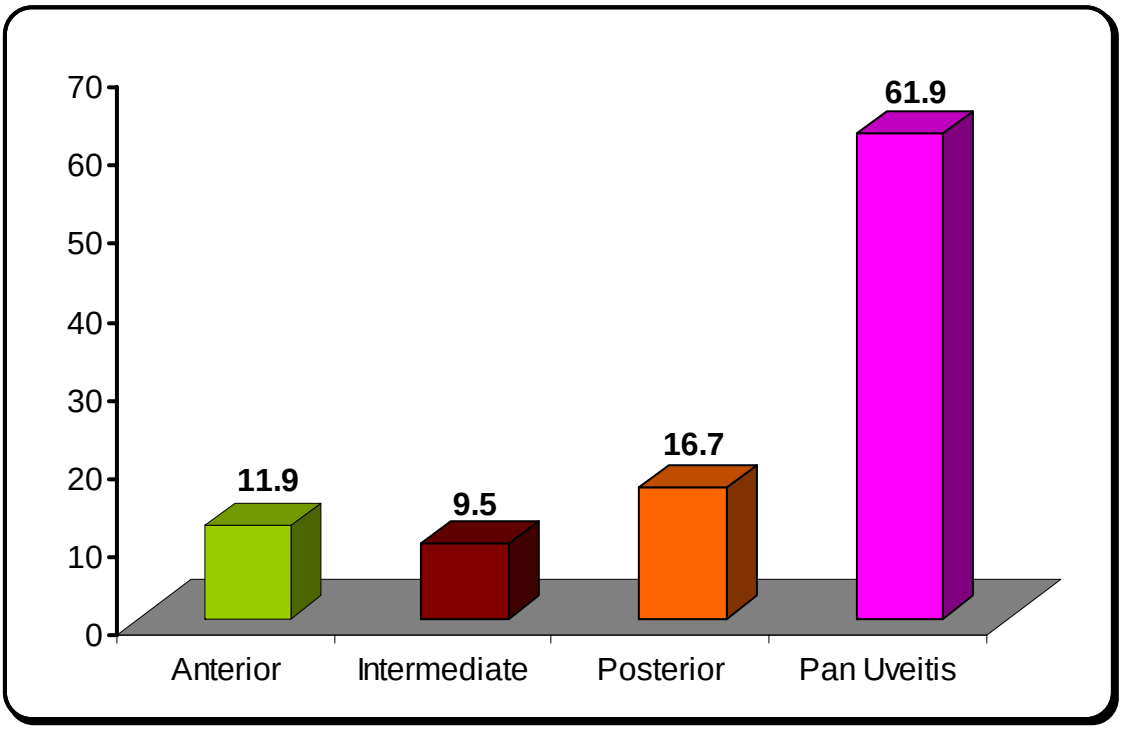

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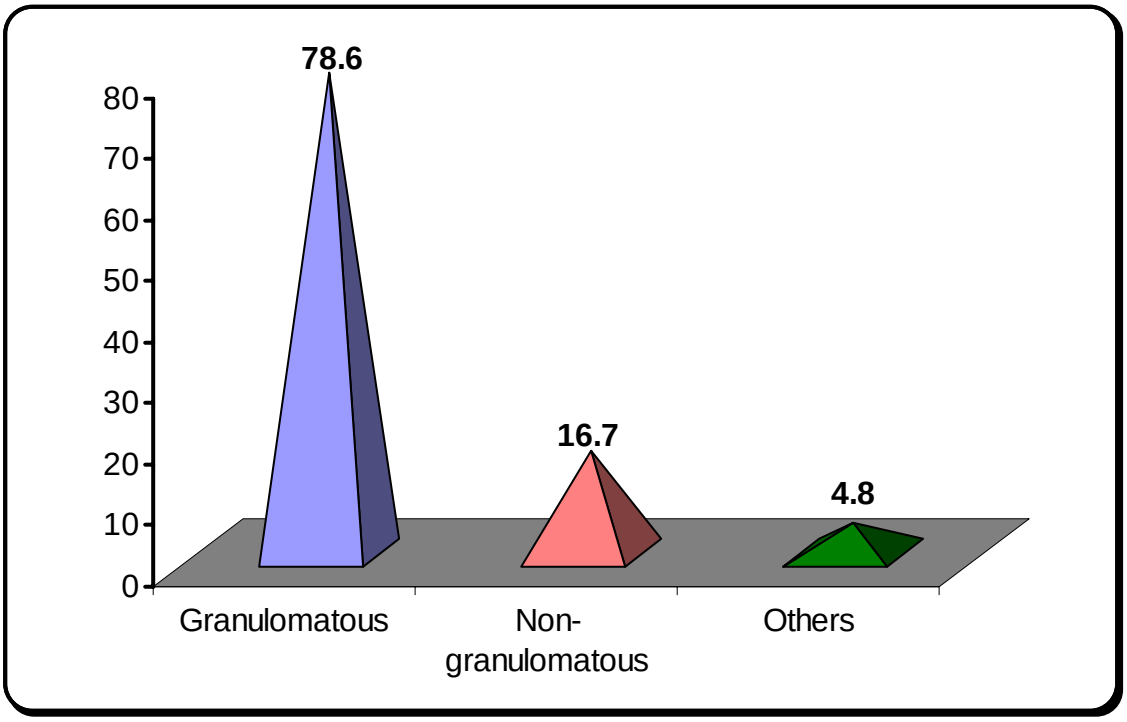
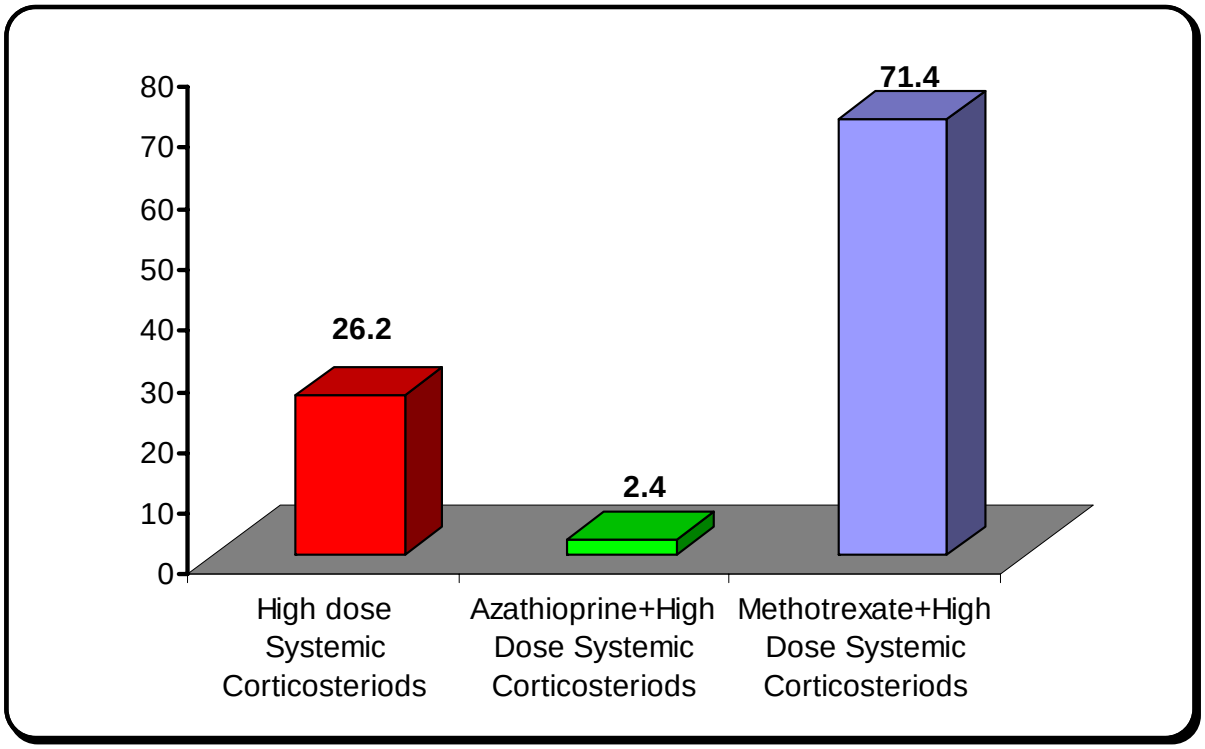


MEDICATION


80
70
60
50
40
30
20
10
0
26.2
2.4
71.4
High dose Systemic Corticosteriods
Azathioprine+High Dose Systemic Corticosteriods
Methotrexate+High Dose Systemic Corticosteriods